REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

I. Status of the Claims and Amendments

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

Claims 1 and 61-67 are currently being amended. Support for these amendments can be found throughout the specification as-filed, including the original claims and page 4, lines 2-3.

After amending the claims as set forth above, claims 1, 54-76, and 78-82 are now pending, and claims 55-60 are withdrawn. Thus, claims 1, 54, 61-76, and 78-81 are pending and subject to examination on the merits.

II. Interview Summary

Applicants appreciate the courtesy extended by the Examiner in granting a personal interview to discuss the application. The Interview Summary dated November 21, 2006, accurately reflects the substance of the interview. As discussed during the interview, Applicants submit with this response a declaration including data in tabular form to establish the unexpected properties of the claimed compounds.

III. Claim Rejections – 35 U.S.C. § 112, First Paragraph

Claims 1, 54, 61-76, and 78-81 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking written description support. According to the Office Action, "[n]o persuasive support could be found in the specification or the originally filed claims for the expression

'bearing at least one nitrogen group' found in claims 1, 62-67 and 69." Office Action at 5. Applicants respectfully traverse this ground of rejection.

While not acquiescing in the propriety of the rejection, Applicants have amended the claims to no longer recite "bearing at least one nitrogen group." Instead, the claims recite a "heteroatom selected from the group consisting of halogen or a nitrogen atom." Support for this amendment can be found throughout the specification as-filed, including the original claims and page 4, lines 2-3. Indeed, the specification is replete with examples of nitrogen and halogen heteroatoms. Because the claims no longer recite the language deemed lacking written description support, Applicants respectfully request withdrawal of this ground of rejection.

IV. Claim Rejections – 35 U.S.C. § 112, Second Paragraph

Claims 61 and 63-65 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Each of the specific grounds of rejection is addressed below.

A. Claim 61

The Office Action rejects claim 61 as allegedly indefinite, because "there are specie listed which are not embraced by independent claim 1." Office Action at 7. The compounds allegedly outside the scope of claim 61 include compounds compound xxv, lxix, ci, cii, and lxii.

While not acquiescing in the propriety of the rejection, Applicants have amended claim 61 to no longer recite the compounds deemed outside the scope of the claim. Accordingly, the amendment renders this ground of rejection moot.

B. Claims 63-65

The Office Action rejects claims 63-365 as allegedly indefinite, because "there is a valence problem with the R substituent 'sulfonyl'." Office Action at 7.

While not acquiescing in the propriety of the rejection, Applicants have amended claims 63-65 to no longer recite "sulfonyl." Thus, the amendment renders the rejection moot.

V. Double Patenting

Claims 1, 54, 61-76, and 78-81 stand "provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 of copending Application No. 10/523,018." Office Action at 7-9.

Applicants note that the double patenting rejection is provisional. Thus, Applicants will address the rejection when, if ever, it becomes a non-provisional rejection.

VI. Claim Rejections – 35 U.S.C. § 103

Claims 1, 54, 61, and 73-76 stand rejected under 35 U.S.C. § 103 as allegedly obvious over the following references, either alone or in any combination:

(a) WO 00/33842 to Lago *et al.*;

(b) U.S. Patent No. 3,467,666 to Dexter *et al.*;

(c) U.S. Patent No. 3,201,409 to Spivack *et al.*;

(d) U.S. Patent No. 6,291,514 to Illig *et al.*;

(e) U.S. Pat. Appl. Pub. No. 2003/0158199 to Steiber *et al.*; and

(f) U.S. Pat. Appl. Pub. No. 2001/0044545 to Dhanoa *et al.*

According to the Office Action, references (a)-(f) "each teach substituted phenylamino-2-thiazole compounds that are structurally similar to the instant claimed compounds." Office Action at 14. The Office Action concludes that one of skill in the art would be motivated to make the specifically claimed compounds "from the expectation that structurally similar compounds would possess similar activity (e.g., antagonizing the myt1 kinase receptor)." *Id.* at 15. Applicants respectfully traverse this ground of rejection.

As discussed below, the Office Action has not established a *prima facie* case of obviousness, because there is no motivation to arrive at the claimed invention. Even if a *prima facie* case of obviousness has been established, the case has been rebutted by Applicants' showing that the claimed compounds exhibit unexpected properties.

A. There Is No Motivation To Arrive At The Claimed Invention

There is not teaching or suggestion in the art to modify references (a)-(f) to arrive at the claimed invention. The Office Action contends that motivation stems "from the expectation that structurally similar compounds would possess similar activity (e.g., antagonizing the myt1 kinase receptor)." However, MYT1 kinase, which belongs to the Casein Kinase 1 family, has structure and properties vastly different from stem-cell factor receptors, such as c-kit. Given this differing structure and properties, one of skill in the art would have no motivation to modify the prior art compounds to discover compounds capable of selectively inhibiting c-kit. Indeed, a skilled artisan would have no reasonable expectation that an antagonist of one compound, MYT1 kinase, would be an inhibitor of another structurally different compound, c-kit. Applicants, however, surprisingly discovered that the presently claimed compounds are potent and selective inhibitors of c-kit (spec. at page 3, lines 7-12), as discussed below in Section B.

The Office Action argues that "motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (e.g., antagonizing the mytl kinase receptor)." Office Action at 15. However, "[t]he mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." MPEP § 2143.01(III); *see also In re Brouwer*, 77 F.3d 422, 425, 37 USPQ2d 1663, 1666 (Fed. Cir. 1996). Here, nothing in the cited references suggests altering the disclosed compounds in such a way to arrive at the claimed compounds. Instead, the Office Action relies on the skilled artisan's hopes that some unknown structurally similar compounds would have the desired activities. Such a hope does not provide the requisite motivation to make the necessary modifications. Even if one of skill in the

art would be motivated to make random modifications in hope of finding a compound with the desired activity, there would be no reasonable expectation of success. *See* MPEP § 2143.02.

B. The Claimed Compounds Have Unexpected Properties

Applicants enclose a declaration by Marco A. Ciufolini, one of the named inventors, under 37 C.F.R. § 1.132 (Ciufolini Declaration) demonstrating unexpected properties of the claimed invention. Specifically, Applicants tested the compound on page 3, line 17 of Lago, the compound of example 13 of Dexter, the compound of example 19 of Spivack, compound 18 of Illig, compound 17 on page 7 and compound 35 on page 10 of Stieber, and compound 24 on page 6 of Dhanoa.[1] *See* Ciufolini Declaration at ¶¶ 5 & 10. The c-kit inhibition activity of these compounds was compared to the activity of the claimed compounds.

None of the compounds cited by the Office Action, except for Lago's compound and Spivack's compound, showed any appreciable c-kit inhibitory activity for any of the different forms of c-kit. Ciufolini Declaration at ¶ 11; Table 1 (pg. 12). The claimed compounds, on the other hand, were selective in inhibiting c-kit. Ciufolini Declaration at ¶ 13 & 14. Nothing in the prior art suggests this selective inhibition of c-kit.

With respect to Lago's compound and Spivack's compound, they lacked the potency and selectivity of the claimed compounds. More specifically, Lago's compound did not discriminate between mutated c-kit and wild type c-kit. Ciufolini Declaration at ¶ 9. Thus, Lago's compound was not a selective c-kit inhibitor. As to Spivack's compound, it showed some activity on one of the c-kit mutants, the delta27 mutant, but the IC50 was 7.5 μM as compared to an IC50 of 0.1 μM for the claimed compound. Ciufolini Declaration at ¶ 11. Thus, the claimed compound was far more potent than Spivack's compound. Accordingly, the claimed compounds demonstrate activity not expected from the prior art.

[1] A compound from Illig was not tested due to the extremely complicated synthetic process required. Ciufolini Declaration at ¶ 12. However, the compound is a 1,4-diamino derivative and also an amidine derivative know to be a protease inhibitor. Thus, Dr. Ciufolini did not expect it to have any activity on c-kit.

This selectivity of the claimed compounds has important practical applications. *See* Ciufolini Declaration at ¶ 15. For example, the high degree of selectivity allows the claimed compounds to be diseases characterized by expression of particular forms of c-kit. *Id.* Expression of wild-type c-kit is associated with conditions, such as inflammatory diseases and autoimmune diseases. Thus, inhibitors of wild-type c-kit can be used to treat these conditions. Expression of mutated c-kit is associated with conditions, such as the aggressive forms of mastocytosis. Thus, inhibitors of mutated forms of c-kit can be used to treat these conditions. *See* Ciufolini Declaration at ¶ 15 & 16. In other words, the selectivity allows the compounds to be clinically applied to treat a variety of conditions implicating c-kit.

Nothing in the prior art suggests that the claimed compounds would possess the selective inhibition of c-kit described in the Ciufolini Declaration. Accordingly, the claimed compounds exhibit unexpected results over the prior art.

For at least these reasons, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

CONCLUSION

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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